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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,021	02/18/2005	Mitsutaka Nakamura	0020-5041PUS2	3141

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EXAMINER	
HUYNH, CARLIC K	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
12/17/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,021	NAKAMURA ET AL.	
	Examiner	Art Unit	
	Carlic K. Huynh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *14-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *18 February 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-19 are pending in the application, with claims 14-19 having been withdrawn, in response to the restriction requirement submitted on August 29, 2007. Accordingly, claims 1-13 are being examined on the merits herein.

Election/Restrictions

2. Applicant's election of the claims of Group I, namely claims 1-13, in the reply filed on October 1, 2007 is acknowledged. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 14-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on October 1, 2007.

Accordingly, claims 1-13 are examined on the merits herein.

The election/restriction requirement is deemed proper and is made FINAL.

Information Disclosure Statement

The Information Disclosure Statement submitted on February 18, 2005, is acknowledged.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract contains legal phraseology, namely "said". Appropriate correction is required. See MPEP 37 CFR § 1.72 (b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommerville et al. (WO 03/066039 A1) in view of Wong et al. (US 6,964,962).

It is noted that (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinyl-methyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptanedicarboximide hydrochloride is known in the art as SM-13496 (see page 7, lines 5-8 of the specification). Thus, SM-13496 is the

hydrochloride salt of (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinyl-methyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptanedicarboximide.

Sommerville et al. teach a method of treating schizophrenia comprising atypical antipsychotics, namely SM-13496 (abstract; and page 5, line 35). Sommerville et al. further teaches positive and negative symptoms are often increased during the acute phase, or the florid psychotic phase, of schizophrinia and that the method of Sommerville et al. is aimed at treatment during the acute phase of schizophrenia (page 4, lines 16-23).

Sommerville et al. do not explicitly teach the dose of SM-13496 (see page 7, lines 23-25).

Wong et al. teach 0.05 to 7500 mg/day/patient of SM-13496 can be used to schizophrenia (see column 4, lines 51-58; and Table in column 8, line 16), which details the daily dose of SM-13496 that can be given to the patient and thus may be a once a day administration.

Moreover, Wong et al. teach 0.05 to 7500 mg/day/patient of SM-13496 can be used to schizophrenia (column 4, lines 51-58; and Table in column 8, line 16). Thus it would be obvious to one skilled in the art that the amount of (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinyl-methyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptanedicarboximide hydrochloride may be optimized to be administered at 5 to 120, 20 to 80, 5 to 80, or 10 to 40 mg once a day. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

Accordingly, absence the showing of unexpected results, it would have been obvious to a person of skill in the art at the time of the invention to employ the composition of Sommerville et al. to contain 0.05 to 7500 mg/day/patient of SM-13496 because the composition of Wong et al.

contains 0.05 to 7500 mg/day/patient of SM-13496 and according to Wong et al., 0.05 to 7500 mg/day/patient of SM-13496 can be used to treat schizophrenia.

The motivation to combine the compounds of Sommerville et al. to the compounds of Wong et al. is that the compositions of Wong et al. are SM-13496 compositions and that such compositions treat schizophrenia.

It is noted that "It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose" and "It is obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose". *In re Kerkhoven*, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Conclusion

5. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

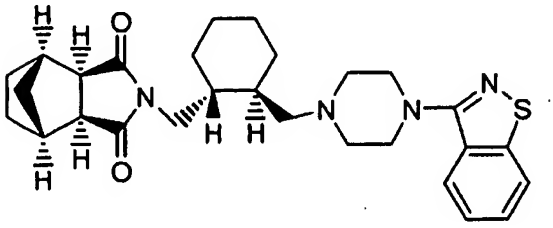
ckh

S. Wang

SHENGJUN WANG
PRIMARY EXAMINER

CLAIMS

1. A method for treatment of schizophrenia without being accompanied by any extrapyramidal symptoms, which comprises orally administering a daily dose of 5 mg to 120 mg of the active compound: (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptanedicarboximide of the formula (1):



(1)

or a pharmaceutically acceptable salt thereof to a patient suffering from schizophrenia once a day.

2. The method for treatment according to claim 1, wherein the active compound is (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]-heptanedicarboximide hydrochloride.

3. The method for treatment according to claim 1 or claim 2, which improves the negative symptoms of schizophrenia.

4. The method for treatment according to claim 1 or claim 2, which improves the positive and negative symptoms of schizophrenia.

5. The method for treatment according to claim 1 or claim 2, which comprises orally administering the active compound: (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptanedicarboximide hydrochloride at a daily dose of 20 mg to 80 mg once a day.

6. The method according to claim 5, which improves the negative symptoms of schizophrenia.

7. The method according to claim 5, which improves the positive and negative symptoms of schizophrenia.

8. The method for treatment of schizophrenia in the chronic stage according to claim 1 or claim 2, which improves schizophrenia without being accompanied by any extrapyramidal symptoms by orally administering the active compound: (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo [2.2.1]heptanedicarboximide hydrochloride at a daily dose of 5 mg to 80 mg once a day.

9. The method for treatment according to claim 8, which improves the negative symptoms of schizophrenia.

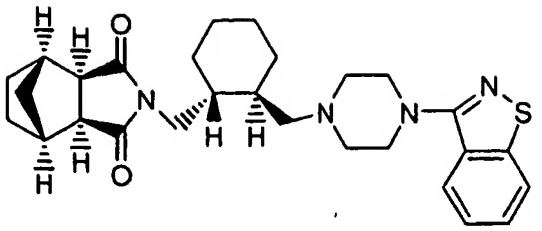
10. The method for treatment according to claim 8, which improves the positive and negative symptoms of schizophrenia.

11. The method for treatment according to claim 8, which comprises orally administering the active compound: (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo[2.2.1]heptanedicarboximide hydrochloride at a daily dose of 10 mg to 40 mg once a day.

12. The method for treatment according to claim 11, which improves the negative symptoms of schizophrenia.

13. The method for treatment according to claim 11, which improves the positive and negative symptoms of schizophrenia.

14. An agent for treatment of schizophrenia, which comprises as an active compound (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo [2.2.1]heptane-dicarboximide of the formula (1):



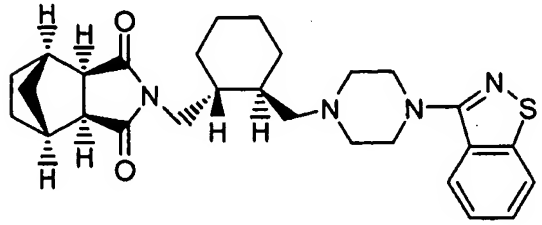
(1)

or a pharmaceutically acceptable salt thereof in an amount of 5 mg to 120 mg as a daily dose for oral administration once a day.

15. The agent according to claim 14, wherein the active compound is (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo [2.2.1]heptane-dicarboximide hydrochloride.

16. The agent according to claim 14 or claim 15, wherein the content of the active compound is in the range of 20 mg to 80 mg.

17. A use of (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinylmethyl]-1-cyclohexylmethyl]-2,3-bicyclo [2.2.1]heptane-dicarboximide of the formula (1):



(1)

or a pharmaceutically acceptable salt thereof in the preparation of an agent for treatment of schizophrenia.

18. The use according to claim 17, wherein the active compound is (1R,2S,3R,4S)-N-[(1R,2R)-2-[4-(1,2-benzoisothiazol-3-yl)-1-piperazinyl-methyl]-1-cyclohexylmethyl]-2,3-bicyclo [2.2.1]heptanedicarboximide hydrochloride.

19. The use according to claim 17 or claim 18, wherein the agent for treatment of schizophrenia contains the active compound in an amount of 5 mg to 120 mg as a daily dose for oral administration once a day.